SEQUENCE LISTING



Bl

<110> KISHIMOTO, Tadamitsu NAGASAWA, Takashi TACHIBANA, Kazunobu CHUGAI SEIYAKU KABUSIKI KAISHA

<120> Vascularization Inhibitors

<130> 46124-5042-US

<140> US 09/646,785

<141> 2001-02-16

<150> PCT/JP99/01448

<151> 1999-03-23

<150> JP10/95448

<151> 1998-03-24

<160> 12

<210> 1

<211> 352

<212> PRT

<213> Mus

<400> 1

Met Glu Gly Ile Ser Ile Tyr Thr Ser Asp Asn Tyr Thr Glu Glu Met Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys Phe Arg 20 25 Glu Glu Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile Tyr 40 35 Ser Ile Ile Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys 70 65 Tyr Arg Leu His Leu Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val Asp Ala Val Ala Asn Trp Tyr Phe Gly 95 100 Asn Phe Leu Cys Lys Ala Val His Val Ile Tyr Thr Val Asn Leu 110 115 Tyr Ser Ser Val Leu Ile Leu Ala Phe Ile Ser Leu Asp Arg Tyr 125 130 Leu Ala Ile Val His Ala Thr Asn Ser Gln Arg Pro Arg Lys Leu 145 140 Leu Ala Glu Lys Val Val Tyr Val Gly Val Trp Ile Pro Ala Leu 155 160 Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asn Val Ser Glu Ala 175 170 Asp Asp Arg Tyr Ile Cys Asp Arg Phe Tyr Pro Asn Asp Leu Trp 185 190 Val Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu Ile Leu

200

RECEIVED
JUL 2 3 2002
TECH CENTER 1600/2900

205

```
Pro Gly Ile Val Ile.Leu Ser Cys Tyr Cys Ile Ile Ile Ser Lys
                                    220
                215
Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr
                                    235
                                                         240
Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr
                                    250
                                                         255
                245
Tyr Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu Ile Ile
                260
                                    265
Lys Gln Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile Ser
                275
                                    280
Ile Thr Glu Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile
                290
                                    295
Leu Tyr Ala Phe Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His
                                    310
Ala Leu Thr Ser Val Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser
                320
                                    325
Lys Gly Lys Arg Gly Gly His Ser Ser Val Ser Thr Glu Ser Glu
                335
Ser Ser Ser Phe His Ser Ser
                350
<210> 2
<211> 1588
<212> DNA
<213> Mus
<220>
<221> CDS
<222> (1)...(1059)
<400> 2
atg gag ggg atc agt ata tac act tca gat aac tac acc gag gaa 45
atg ggc tca ggg gac tat gac tcc atg aag gaa ccc tgt ttc cgt 90
gaa gaa aat gct aat ttc aat aaa atc ttc ctg ccc acc atc tac 135
tcc atc atc ttc tta act ggc att gtg ggc aat gga ttg gtc atc 180
ctq qtc atq gqt tac cag aag aaa ctg aga agc atg acg gac aag 225
tac agg ctg cac ctg tca gtg gcc gac ctc ctc ttt gtc atc acg 270
ctt ccc ttc tgg gca gtt gat gcc gtg gca aac tgg tac ttt ggg 315
aac tto cta tgc aag gca gtc cat gtc atc tac aca gtc aac ctc 360
tac age agt gtc ctc atc ctg gcc ttc atc agt ctg gac cgc tac 405
ctg gcc atc gtc cac gcc acc aac agt cag agg cca agg aag ctg 450
ttq qct qaa aag gtg gtc tat gtt ggc gtc tgg atc cct gcc ctc 495
ctg ctg act att ccc gac ttc atc ttt gcc aac gtc agt gag gca 540
gat gac aga tat atc tgt gac cgc ttc tac ccc aat gac ttg tgg 585
gtg gtt gtg ttc cag ttt cag cac atc atg gtt ggc ctt atc ctg 630
cct ggt att gtc atc ctg tcc tgc tat tgc att atc atc tcc aag 675
ctg tca cac tcc aag ggc cac cag aag cgc aag gcc ctc aag acc 720
aca gtc atc ctc atc ctg gct ttc ttc gcc tgt tgg ctg cct tac 765
tac att ggg atc agc atc gac tcc ttc atc ctc ctg gaa atc atc 810
aag caa ggg tgt gag ttt gag aac act gtg cac aag tgg att tcc 855
atc acc gag gcc cta gct ttc ttc cac tgt tgt ctg aac ccc atc 900
ctc tat gct ttc ctt gga gcc aaa ttt aaa acc tct gcc cag cac 945
gca etc ace tet gtg age aga ggg tee age etc aag ate etc tee 990
aaa gga aag cga ggt gga cat tca tct gtt tcc act gag tct gag 1035
tct tca agt ttt cac tcc agc taa cacagatgta aaagactttt ttttat 1085
acgataaata acttttttt aagttacaca tttttcagat ataaaagact gaccaatatt 1145
```

```
gtacagtttt tattgcttgt tggatttttg tcttgtgttt ctttagtttt tgtgaagttt 1205
aattgactta tttatataaa tttttttgt ttcatattga tgtgtgtcta ggcaggacct 1265
gtggccaagt tcttagttgc tgtatgtctc gtggtaggac tgtagaaaag ggaactgaac 1325
attccagagc gtgtagttaa tcacgtaaag ctagaaatga tccccagctg tttatgcata 1385
gataatctct ccattcccgt ggaacgtttt tcctgttctt aagacgtgat tttgctgtag 1445
aagatggcac ttataaccaa agcccaaagt ggtatagaaa tgctggtttt tcagtttca 1505
ggagtgggtt gattcagca cctacagtgt acagtcttgt attaagttgt taataaaagt 1565
acatgttaaa cttaaaaaaa aaa 1588

<210> 3
<211> 359
<212> PRT
```

<213> Mus <400> 3 Met Glu Pro Ile Ser Val Ser Ile Tyr Thr Ser Asp Asn Tyr Ser Glu Glu Val Gly Ser Gly Asp Tyr Asp Ser Asn Lys Glu Pro Cys Phe Arg Asp Glu Asn Val His Phe Asn Arg Ile Phe Leu Pro Thr Ile Tyr Phe Ile Ile Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile Leu Val Met Gly Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr Arg Leu His Leu Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro Phe Trp Ala Val Asp Ala Met Ala Asp Trp Tyr Phe Gly Lys Phe Leu Cys Lys Ala Val His Ile Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Ala Val Tyr Val Gly Val Trp Ile Pro Ala Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asp Val Ser Gln Gly Asp Ile Ser Gln Gly Asp Asp Arg Tyr Ile Cys Asp Arg Leu Tyr Pro Asp Ser Leu Trp Met Val Val Phe Gln Phe Gln His Ile Met Val Gly Leu Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys Ile Ile Ile Ser Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys Ala Leu Lys Thr Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp Leu Pro Tyr Tyr Val Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Gly Val Ile Lys Gln Gly Cys Asp Phe Glu Ser Ile Val His Lys Trp Ile Ser Ile Thr Glu Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe Leu Gly Ala Lys

```
315
               305.
Phe Lys Ser Ser Ala Gln His Ala Leu Asn Ser Met Ser Arg Gly
                                   325
               320
                            .
Ser Ser Leu Lys Ile Leu Ser Lys Gly Lys Arg Gly Gly His Ser
               335
                                   340
Ser Val Ser Thr Glu Ser Glu Ser Ser Phe His Ser Ser
               350
<210> 4
<211> 1758
<212> DNA
<213> Mus
<220>
<221> CDS
<222> (1)...(1080)
<223>
<400> 4
atg gaa ccg atc agt gtg agt ata tac act tct gat aac tac tct 45
gaa gaa gtg ggg tct gga gac tat gac tcc aac aag gaa ccc tgc 90
ttc cgg gat gaa aac gtc cat ttc aat agg atc ttc ctg ccc acc 135
atc tac ttc atc ttc ttg act ggc ata gtc ggc aat gga ttg 180
gtg atc ctg gtc atg ggt tac cag aag aag cta agg agc atg acg 225
gac aag tac egg etg cac etg tea gtg get gac etc etc ttt gte 270
ate aca etc ecc ttc tgg gea gtt gat gec atg get gac tgg tac 315
ttt ggg aaa ttt ttg tgt aag gct gtc cat atc atc tac act gtc 360
aac etc tac age age gtt etc atc etg gee tte atc age etg gae 405
cgg tac ctc gcc att gtc cac gcc acc aac agt caa agg cca agg 450
aaa ctg ctg gct gaa aag gca gtc tat gtg ggc gtc tgg atc cca 495
gcc ctc ctc ctg act ata cct gac ttc atc ttt gcc gac gtc agc 540
cag ggg gac atc agt cag ggg gat gac agg tac atc tgt gac cgc 585
ctt tac ccc gat agc ctg tgg atg gtg ttt caa ttc cag cat 630
ata atg gtg ggt ctc atc ctg ccc ggc atc gtc atc ctc tcc tgt 675
tac tgc atc atc tct aag ctg tca cac tcc aag ggc cac cag 720
aag cgc aag gcc ctc aag acg aca gtc atc ctc atc cta gct ttc 765
ttt gcc tgc tgg ctg cca tat tat gtg ggg atc agc atc gac tcc 810
ttc atc ctt ttg gga gtc atc aag caa gga tgt gac ttc gag agc 855
att gtg cac aag tgg atc tcc atc aca gag gcc ctc gcc ttc ttc 900
cac tgt tgc ctg aac ccc atc ctc tat gcc ttc ctc ggg gcc aag 945
ttc aaa agc tct gcc cag cat gca ctc aac tcc atg agc aga ggc 990
tcc agc ctc aag atc ctt tcc aaa gga aag cgg ggt gga cac tct 1035
tcc gtc tcc acg gag tca gaa tcc tcc agt ttt cac tcc agc taa 1080
cccttatgca aagacttata taatatatat atatatatga taaagaactt ttttatgtta 1140
cacattttcc agatataaga gactgaccag tcttgtacag ttttttttt tttttaattg 1200
actgttggga gtttatgttc ctctagtttt tgtgaggttt gacttaattt atataaatat 1260
tgttttttgt ttgtttcatg tgaatgagcg tctaggcagg acctgtggcc aagttcttag 1320
tagctgttta tctgtgtgta ggactgtaga actgtagagg aagaaactga acattccaga 1380
atgtgtggta aattgaataa agctagccgt gatcctcagc tgttgctgca taatctcttc 1440
attocgagga gcaccccacc cccacccca cccccacccc attottaaat tgtttggtta 1500
aagatggcac ttaaaaccaa agcctgaaat ggtggtagaa atgctggggt ttttttttgtt 1620
tqtttqtttt ttcaqttttc aaqaqtaqat tqacttcagt ccctacaaat gtacagtctt 1680
gtattacatt qttaataaaa qtcaatgata aacttaaaaa aaaaaaaaaa aaaaaaaaa 1740
aaaaaaaaa aaaaaaaa
                                                                1758
```

```
<210> 5
<211> 89
<212> PRT
<213> Artificial Sequence
<220>
<223> Ligand peptide
<400> 5
Met Asn Ala Lys Val Val Val Leu Val Leu Val Leu Thr Ala
                                    10
Leu Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys
Pro Cys Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys
                                    40
                                                       45
                35
His Leu Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val
                50
                                    55
Ala Arg Leu Lys Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys
                                                       75
                65
                                    7û
Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys
<210> 6
<211> 2244
<212> DNA
<213> Mus
<220>
<221> CDS
<222> (471)...(743)
<400> 6
gcacgggaca ggccgggcca cacccaccgg ggcgagctcg gagggcggcg ctctgggcgg 60
agggcccggc ggctcggcc agggcgcgtt acctcgtcgc cggggccgga gagggcgggc 120
ggaggcacgg ggcctggagg cgccaggcgg aggatgcggg cgacacggtg gcggcggcga 180
ggatctgtcg aggaaaaatc ttgcggccgg cgattccccg ccttttaagc gcagcctgca 300
ctcccccac cccacgcagg ggcgggcctt ccccaacgcg ggcgcccact ggccgccgcg 360
egeogetece etecageteg cetgegeete teacteteeg teageegeat tgecegeteg 420
gegteeggee eeegaceege getegteege eegeeegee geeegeege gee 473
atg aac gcc aag gtc gtg gtc gtg ctg gtc ctc gtg ctg acc gcg 518
ctc tgc ctc agc gac ggg aag ccc gtc agc ctg agc tac aga tgc 563
cca tgc cga ttc ttc gaa agc cat gtt gcc aga gcc aac gtc aag 608
cat ctc aaa att ctc aac act cca aac tgt gcc ctt cag att gta 653
gcc cgg ctg aag aac aac aga caa gtg tgc att gac ccg aag 698
cta aag tgg att cag gag tac ctg gag aaa gct tta aac aag taa 743
gcacaacagc caaaaaggac tttccgctag acccactcga ggaaaactaa aaccttgtga 803
gagatgaaag ggcaaagacg tgggggaggg ggccttaacc atgaggacca ggtgtgtgtg 863
tggggtgggc acattgatct gggatcgggc ctgaggtttg ccagcattta gaccctgcat 923
ttatagcata cggtatgata ttgcagctta tattcatcca tgccctgtac ctgtgcacgt 983
tggaattttt attactgggg tttttctaag aaagaaattg tattatcaac agcattttca 1043
agcagttagt tccttcatga tcatcacaat catcatcatt ctcattctca ttttttaaat 1103
caacgagtac ttcaagatct gaatttggct tgtttggagc atctcctctg ctcccctggg 1163
gagtctgggc acagtcaggt ggtggcttaa cagggagctg gaaaaagtgt cctttcttca 1223
gacactgagg ctcccgcagc agcgcccctc ccaagaggaa ggcctctgtg gcactcagat 1283
```

```
accqactggg gctgggcgcc gccactgcct tcacctcctc tttcaacctc agtgattggc 1343
tctgtgggct ccatgtagaa gccactatta ctgggactgt gctcagagac ccctctccca 1403
gctattccta ctctcccc gactccgaga gcatgcatta atcttgcttc tgcttctcat 1463
ttctgtagcc tgatcagcgc cgcaccagcc gggaagaggg tgattgctgg ggctcgtgcc 1523
ctgcatccct ctcctcccag ggcctgcccc acagctcggg ccctctgtga gatccgtctt 1583
tggcctcctc cagaatggag ctggccctct cctggggatg tgtaatggtc cccctgctta 1643
cccqcaaaaq acaaqtcttt acaqaatcaa atgcaatttt aaatctgaga gctcgctttg 1703
agtgactggg ttttgtgatt gcctctgaag cctatgtatg ccatggaggc actaacaaac 1763
tctgaggttt ccgaaatcag aagcgaaaaa atcagtgaat aaaccatcat cttgccacta 1823
cccctcctg aagccacagc agggtttcag gttccaatca gaactgttgg caaggtgaca 1883
tttccatgca taaatgcgat ccacagaagg tcctggtggt atttgtaact ttttgcaagg 1943
cattttttta tatatattt tgtgcacatt tttttttacg tttctttaga aaacaaatgt 2003
atttcaaaat atatttatag tcgaacaatt catatatttg aagtggagcc atatgaatgt 2063
caqtaqttta tacttctcta ttatctcaaa ctactggcaa tttgtaaaga aatatatatg 2123
atatataaat gtgattgcag cttttcaatg ttagccacag tgtatttttt cacttgtact 2183
aaaattgtat caaatgtgac attatatgca ctagcaataa aatgctaatt gtttcatggt 2243
                                                                   2244
<210> 7
<211> 89
<212> PRT
<213> Artificial Sequence
<220>
<223> Ligand peptide
<400> 7
Met Asp Ala Lys Val Val Ala Val Leu Ala Leu Val Leu Ala Ala
                                                         15
                                     10
Leu Cys Ile Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys
                 20
                                     25
                                                          30
Pro Cys Arg Phe Phe Glu Ser His Ile Ala Arg Ala Asn Val Lys
                                                         45
                 35
                                     40
His Leu Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val
                 50
                                     55
Ala Arg Leu Lys Asn Asn Arg Gln Val Cys Ile Asp Pro Lys
                                     70
                                                          75
Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys
<210> 8
<211> 1781
<212> DNA
<213> Mus
<220>
<221> CDS
<222> (82)...(351)
<400> 8
gaccactttc cctctcggtc cacctcggtg tcctcttgct gtccagctct gcagcctccg 60
gcgcgccctc ccgcccacgc c
atg gac gcc aag gtc gtc gcc gtg ctg gcc ctg gtg ctg gcc gcg 126
ctc tgc atc agt gac ggt aaa cca gtc agc ctg agc tac cga tgc 171
ccc tgc cgg ttc ttc gag agc cac atc gcc aga gcc aac gtc aag 216
```

```
cat ctg aaa atc ctc.aac act cca aac tgt gcc ctt cag att gtt 261
gca cgg ctg aag aac aac aga caa gtg tgc att gac ccg aaa 306
tta aag tgg atc caa gag tac ctg gag aaa gct tta aac aag taa 351
qcacaacaqc ccaaaqqact ttccaqtaqa cccccgagga aggctgacat ccgtgggaga 411
tgcaagggca gtggtgggga ggagggcctg aaccctggcc aggatggccg gcgggacagc 471
actgactggg qtcatqctaa qqtttgccag cataaagaca ctccgccata gcatatggta 531
cqatattqca qcttatattc atccctqccc tcqcccgtgc acaatggagc ttttataact 591
ggggtttttc taaggaattg tattacccta accagttagc ttcatcccca ttctcctcat 651
cctcatcttc attttaaaaa gcagtgatta cttcaagggc tgtattcagt ttgctttgga 711
gcttctcttt gccctggggc ctctgggcac agttatagac ggtggctttg cagggagccc 771
tagagagaaa ccttccacca gagcagagtc cgaggaacgc tgcagggctt gtcctgcagg 831
gggcgctcct cgacagatgc cttgtcctga gtcaacacaa gatccggcag agggaggctc 891
ctttatccag ttcagtgcca gggtcgggaa gcttccttta gaagtgatcc ctgaagctgt 951
gctcagagac cctttcctag ccgttcctgc tctctgcttg cctccaaacg catgcttcat 1011
ctgacttccg cttctcacct ctgtagcctg acggaccaat gctgcaatgg aagggaggag 1071
agtgatgtgg ggtgcccct ccctctctc cctttgcttt cctctcactt gggccctttg 1131
tgagattttt ctttggcctc ctgtagaatg gagccagacc atcctggata atgtgagaac 1191
atgcctagat ttacccacaa aacacaagtc tgagaattaa tcataaacgg aagtttaaat 1251
gaggatttgg accttggtaa ttgtccctga gtcctatata tttcaacagt ggctctatgg 1311
gctctgatcg aatatcagtg atgaaaataa taataataat aataataacg aataagccag 1371
aatottgcca tgaagccaca gtggggattc tgggttccaa tcagaaatgg agacaagata 1431
aaacttgcat acattcttat gatcacagac ggccctggtg gtttttggta actatttaca 1491
aggcattttt ttacatatat ttttgtgcac tttttatgtt tctttggaag acaaatgtat 1551
ttcagaatat atttgtagtc aattcatata tttgaagtgg agccatagta atgccagtag 1611
atatctctat gatcttgagc tactggcaac ttgtaaagaa atatatatga catataaatg 1671
tattgtagct ttccggtgtc agccacggtg tatttttcca cttggaatga aattgtatca 1731
actgtgacat tatatgcact agcaataaaa tgctaattgt ttcatgctgt
<210> 9
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> added peptide
<400> 9
Arg Phe Lys Met
<210>10
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> added peptide
<400> 10
Arg Leu Lys Met
<210> 11
<211> 27
<212> DNA
<213> Artificial Sequence
```

764

```
Blanded
Manuage
```

```
<220>
<223> primer

<400> 11
tagcggccgc gttgccatgg aaccgat 27

<210> 12
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> primer

<400> 12
gcgtcgactt tgcataaggg ttagctg 27
```